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Preformulation Studies of Econazole: A Vital Part of Formulation Design

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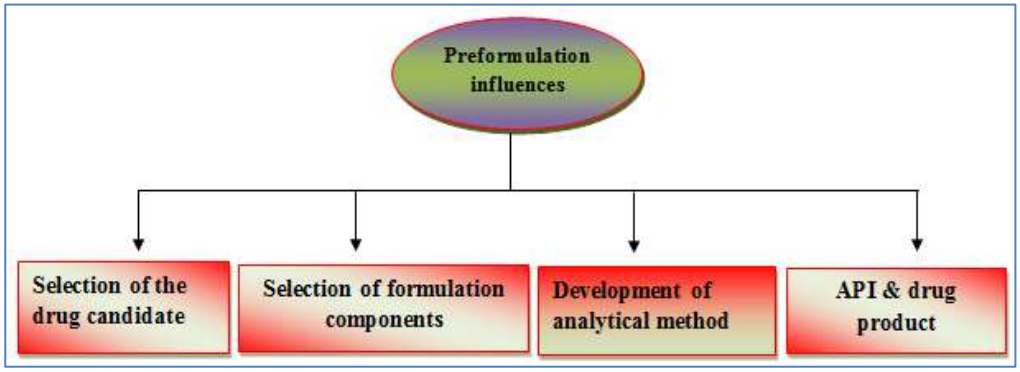
Abstract **Original Research Article**

Preformulation study is a part which is initiated formerly the new molecule is seeded. In a broader way, it pact with studies of physical, chemical, analytical, and pharmaceutical properties related to molecule and provides idea about suitable modification in molecule to show a better performance. Preformulation parameters study can be linked to production of effective, safer, stable, and reliable pharmaceutical formulation. Econazole is a topical imidazole antifungal. It is active against Candida albicans, Malassezia furfur, Microsporum species, Trichophyton species, and Epidermophyton floccosum.

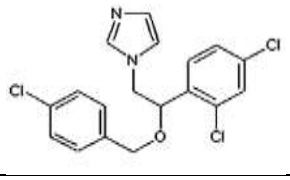
Keywords: Preformulation study, Econazole, Solubility & analytical methods.

INTRODUCTION

Preformulation study is the basic tread in the rational development of dosage forms of a drug substance. The study includes an examination of physical and chemical properties of a drug substance alone and with combined with excepient. The general attempt of preformulation testing is to generate information helpful to the formulator in developing stable and bioavailable dosage forms that can be mass produced. Preformulation investigations are designed to deliver all necessary data especially physicochemical, physico-mechanical and bio pharmaceutical properties of drug substances, excipients and packaging materials [1]. These studies should spotlight on those physicochemical properties of the new compound that could affect drug performance and development of an efficient dosage form. A systematic understanding of these properties may eventually provide a rational for formulation design, or sustain the need for molecular modification. The plan of this study was to establish some of the physicochemical properties such as solubility, melting point, pKa, dissolution, assay development, stability in solution etc [2-3].



Econazole is a topical imidazole antifungal. Econazole inhibits fungal cytochrome P450 sterol c-14 alpha-demethylation. This action blocks the conversion of lanosterol to ergosterol, an integral part of fungal membranes. It is active against Candida albicans, Malassezia furfur, Microsporum species, Trichophyton species, and Epidermophyton floccosum. It also has in vitro activity but has not been clinically validated against T verrucosum, C guillermondii, C parapsilosis, and C tropicalis. Econazole is approved by the FDA for the treatment of tinea pedis, tinea cruris, tinea corporis, tinea versicolor, and cutaneous candidiasis [4].

Drug (Econazole) description [5-7]	
IUPAC Name	1-[2-[(4-chlorophenyl)methoxy]-2-(2,4-dichlorophenyl)ethyl]imidazole
Structure	
Molecular formula	$C_{18}H_{15}Cl_3N_2O$
Molecular Weight	Mass: 381.68 g/mol
Nature	Solid, white & odorless
Solubility	Freely sparingly soluble in ethanol, methanol, and water and practically insoluble in water.
Therapeutic category	Antifungal

In the present works a challenge was made to study preformulation parameters of Econazole which helps to produce information useful in developing stable and Bioavailable dosage forms.

MATERIAL AND METHODOLOGY

Procurement of Drug: Econazole was obtained as gift sample from Qualikems laboratory reagent, New Delhi.

Organoleptic properties

Organoleptic properties of the drug sample were studied by visual inspection.

Preformulation studies [8-11]

Identification of Drug

Melting Point Determination

To determine the M.P. of drug powder, it was filled in a capillary tube with one end open and the other end closed and then the capillary was placed in a digital melting point apparatus.

Solubility

The drug was found to be freely soluble in water and in methanol, very slightly soluble in acetone, which matches the existing reference.

Loss on drying

The average LOD (%w/w) and % LOD were determined.

Partition coefficient

About 50mg of drug was dissolved in 50ml of distilled water and n-octanol separately and both the solution was mixed together by using wrist watch shaker for 30 min. Then the solution was kept in a separating funnel until two phases separated. The aqueous phase was then filtered through the filter paper and was diluted 100 times. The absorbance of both the solutions was taken at 234nm by using UV spectrophotometer. The concentration of drug was determined with the help of standard curve and partition coefficient was determined by following formula:

Analytical Method

UV Spectroscopy of drug performed on UV visible spectrophotometer at the UV -spectrophometer (Model: UV – 1700 Shimadzu) for performing this analysis serial dilution of different concentration of Econazole (10 µg/ml, 15 µg/ml,20 µg/ml,and25,30,35µg/ml) were prepared. Then observed absorbance of different concentrations of dilution and taken U.V. spectra at 267nm of Econazole then plotted calibration graph of the Econazole.

FTIR spectroscopy studies

FTIR (ATR Bruker, Germany) was used. The IR spectrum was obtained by scanning it in the range 4000-500nm and compared with the reference pharmacopoeia (IP-2014).

Table-1: Preformulation Characteristics

S.No.	Characteristics	Results
1.	Appearance	White, bitter, Solid
2.	Melting Point	Melting Point was found to be 163-165ºC.
3.	Partition coefficient	4.78

Table 2: Solubility data of the drug in different solvents/ buffers

S.No.	Solvents	Econazole solubility
1	Water	Slightly soluble
2	0.1 N NaOH	Soluble
3	Acetone	Soluble
4	Ethanol	Slightly soluble
5	Benzene	Soluble
6	Chloroform	Sparingly soluble

Table 3: Percent loss on drying of Econazole

S. No.	wt. of before drying(gm)	wt. of after drying(gm)	LOD(%w/w)	Average LOD(%w/w)	Limit of LOD(%w/w)
1	1	0.9986	0.11	0.14	0.1-0.4
2	1	0.9986	0.13		
3	1	0.9985	0.14		

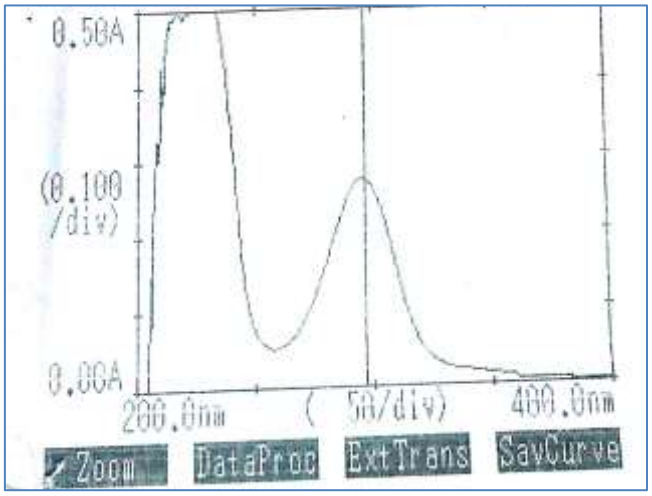


Fig-1: UV Spectra of drug of econazole

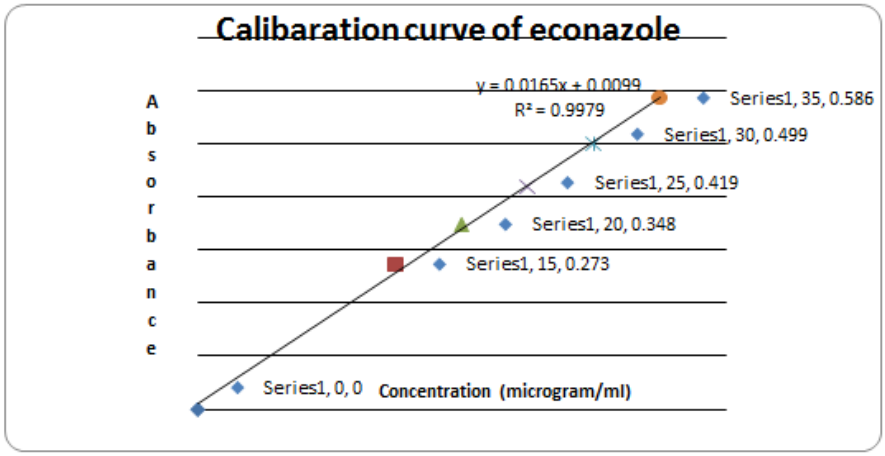


Fig-2: Graph showing caliberation curve of econazole

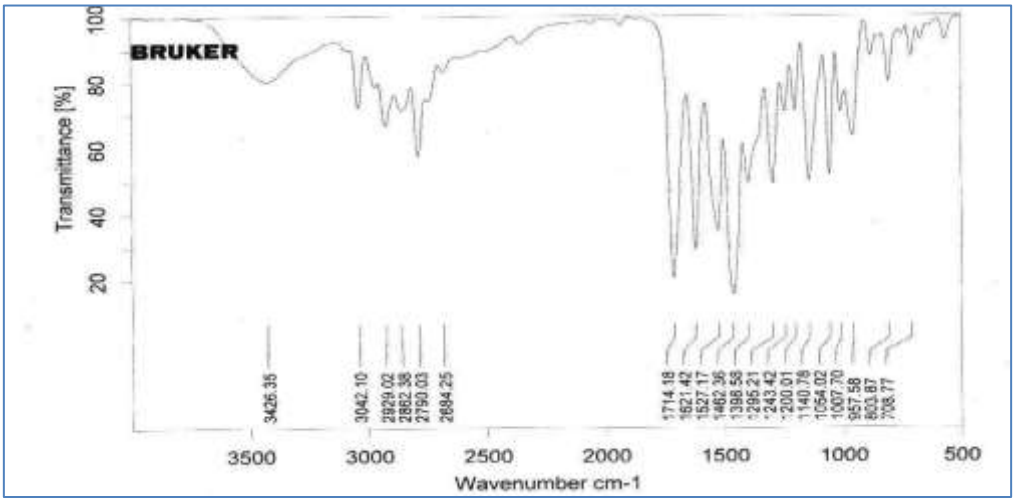


Fig-3: IR spectra of Econazole (sample)

Table-4: Interpretation of IR spectrums

Obtained peak values(cm^{-1})	Functional group
3427	N-H stretch
3109	Aromatic C-H stretch
1585	NO_2 stretch
1547	C=C
3109	C-N stretch
638	C-Cl stretch

RESULTS AND DISCUSSION

The in broad purpose of the present work was to examine preformulation studies of Econazole is to generate information constructive in developing stable and Bioavailable dosage forms. Preformulation studies of drug were undertaken concerning melting point, solubility analysis, UV-spectrophotometric analysis and FTIR analysis to identify and evaluation of purity of drug. Various Preformulation Characteristics were tabulated in table 1. The partition coefficient of rutin was found 4.78, which confirms the lipophilicity of the drug. The drug was found to be freely soluble in water and in methanol, very slightly soluble in acetone, which matches the existing reference. From the result reported in the table 3 revealed that the loss of drying of the drug is within range 0.1-0.4. The analytical method for determination of drug was UV spectroscopy. The absorption spectral analysis showed the λ_{max} of Econazole at 267nm (Fig.1-2). The FTIR spectrum, there was no variation in the Econazole peaks from the standard spectrum of IP 2014(fig 4).The result of interpretation of IR spectra was tabulated in table 4 . Preformulation studies revealed the purity of the drug. UV-spectrophotometric analysis of drug in distilled water ($y = 0.156x + 0.0099$, $R^2 = 0.9979$ revealed the suitability of the standard curve for further calculation.

CONCLUSION

The preformulation tread is a fundamental fraction in establishing the properties of drug that will allow appropriate hazard assessment for development. Frequently it begins all through the lead optimization phase, continues through predomination, and on into the early on phases of development. Consequently, it is compulsory that preformulation should be performed as carefully as possible to facilitate coherent decisions to be made. The preformulation study of Econazole is to make information useful in developing stable and Bioavailable dosage forms.

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